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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,450	11/27/2000	Wolfgang Fleischer	228.1007	9935

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,450	FLEISCHER ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, PhD	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and the filing of RCE both dated 12-29-03 are acknowledged.

Claims included in the prosecution are 22, 32-33, 36-41, 51, 55-61 and 64-74.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22, 32-33, 36-41, 51, 55-61 and 64-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of bacterial infections using liposome encapsulated povidone iodine, does not reasonably provide enablement for generic 'infections' and various compounds recited in claim 70. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d, 1400 (Fed.Cir.1988). Among these factors are: (1) the nature of the invention; 2) the state of the prior art; 3) the relative skill of those in the art; 4) the predictability or unpredictability of the art; 5) the breadth of the claims; 6) the amount of direction or guidance presented; 7) the presence or absence of working examples; and 8) the quantity of experimentation necessary. When the above factors are weighed, it is

the examiners position that one skilled in the art could not practice the invention without undue experimentation.

1) The nature of the invention: the invention concerns with treatment of lower respiratory tract infections using liposomally encapsulated povidone iodine and various compounds such as oxygen releasing compounds, mercury compounds, formaldehyde releasing compounds and others as recited in claim 70.

2) The state of the prior art: the state of the prior art is very high in terms of formulating the liposomal sustained release compositions and the prevention of bacterial infections using povidone-iodine.

3) The relative skill of those in the art: the skill of one of ordinary skill in the art is very high (Ph.D level technology).

4) The predictability or unpredictability in the art: while there is general predictability in formulating the liposomally encapsulated active agents, there is unpredictability in the art of the treatment of viral and fungal diseases using povidone-iodine and compounds in claim 70.

5). The breadth of the claims: instant claims are very broad in terms of the active agents and the microbial diseases to be treated. Claim 70 in particular does not even recite any specific active agent. As pointed out above, claim 70 recites oxygen releasing compounds, mercury compounds, formaldehyde releasing compounds and some of these compounds might be toxic.

6) The amount of direction of guidance provided: instant specification provides no guidance at all in terms of what compounds fall within the generic terms employed in

claim 70 and what specific organisms are killed using these compounds and even povidone-iodine.

7) The presence or absence of working examples: the only examples in the specification pertain to in vitro studies on staphylococcus aureus and herpes simplex type I using only povidone-iodine. There are no in vivo examples at all.

8) The quantity of experimentation necessary: since instant specification does not specify against which specific organisms, povidone-iodine is effective and since the specification does not list the specific compounds which fall under the generic terms as recited in claim 70 and which organisms these compounds are effective, it is difficult for one of ordinary skill in the art to choose the proper active agent and treat the lung diseases without undue experimentation.

3.The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 65-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims recite trachea and bronchi as the tissues; since these belong to the upper respiratory tract, these claims are inconsistent with the parent claim, which recites lower respiratory tract.

Double Patenting

5. The obviousness type double patenting rejection over the claims of 09/701,220 as set forth in the previous office action is maintained in abeyance to the filing of terminal disclaimer.

Claim Rejections - 35 U.S.C. ' 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 22, 32-33, 36-41, 51, 55-61 and 64-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP (0639373) in combination with either knight (5,049,388) or Radhakrishnan (5,049,389) or Prince (5,290,540); or vice versa (Knight or Radhakrishnan or Prince each in view of EP).

EP teaches the same composition. The composition contains liposome encapsulated povidone iodine (abstract and entire article). What is lacking in EP is the

teaching of the application of the composition to treat the infections of lower respiratory tract caused by microbes. However, EP teaches the administration of the composition to mucous membranes (page 2, lines 1-3).

As pointed out before. Knight discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-5 microns. The drugs include antibiotics, antiviral agents and steroids (note the abstract, Tables I and II, examples and claims).

As also pointed out before, Radhakrishnan discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-5 microns. The drugs include antibiotics, antiviral agents and steroids (note the abstract, Examples and claims).

Prince discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-10 microns. The drug combination includes antibiotics, antiviral agents and steroids (note the abstract, Examples and claims).

In the absence of showing unexpected results, it is deemed obvious to one of ordinary skill in the art to use an anti-septic agent and a wound healing promoting agent (encapsulated in liposomes) taught by EP to any part of the body including the respiratory tract, which has a microbial infection and a wound with the expectation of reasonable success since the references of Knight, Radhakrishnan and Prince show the common knowledge in the art of using a combination even for the respiratory tract. One of ordinary skill in the art would have been motivated to use PVP-iodine taught by EP as a drug in the liposomal compositions of Knight, Radhakrishnan or Prince with the

expectation of obtaining similar results since PVP-Iodine is a known anti-septic agent as shown by EP. EP also does not teach the administration of the composition for the infections which occur during remodeling or repairing the lower respiratory tract. However, it is deemed obvious to one of ordinary skill in the art that the wound healing compositions can be applied during any state wherein the wounds are susceptible to infectious agents, with the expectation of similar anti-septic effect.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant once again argues that Knight, Radhakrishnan and Prince are directed to inhalable preparations and EP reference is directed to compositions and methods for external use and therefore, the examiner has not met the requirements for a prima facie rejection for obviousness. The examiner disagrees and points out that although the secondary references do not teach povidone iodine, they show the safety and effectiveness of the liposomes containing the anti-microbial compounds in treating infectious lung diseases. As pointed out before, although the composition in EP is for external use, EP clearly teaches on page 2, lines 1-9 that the preparations are meant for application to the mucous membranes in humans and furthermore, EP is directed to the treatment of eye conditions. This is suggestive of the safe application of the compositions even for nasal or oral or tracheal mucous tissues. Furthermore, EP at the same location teaches that different antibiotics and antiseptic agents are known for the topical treatment of infectious diseases and that while antibiotics quite often lead to patient sensibilization, antiseptic agents such as PVP-iodine can prevent resistances and that they are much more rarely allergenic, as compared to antibiotics. The safe

nature and the effectiveness of the liposomes and the safe nature of the anti-microbial povidone iodine is obvious from the combined teachings of the references and hence one of ordinary skill in the art would be motivated to use the compositions containing PVP-iodine of EP by inhalation route taught by Knight or Radhakrishnan or Prince. For the same reason, applicant's comparison of liposome encapsulated iodine to shampoos and soaps are not persuasive. Furthermore, the examiner points out that applicant himself has not demonstrated the safety and effectiveness of the composition when administered internally. Instant specification contains only in vitro data, that too against a single organism. It is interesting to note that in instant claim applicant recites 'mercury containing compound' and 'formaldehyde releasing compound'. Aren't these compounds toxic to humans?

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

8. Claims 22, 32-33, 36-41, 51, 55-61 and 64-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP (0639373) in combination with either knight (5,049,388)

or Radhakrishnan (5,049,389) or Prince (5,290,540); or vice versa (Knight or Radhakrishnan or Prince each in view of EP) as set forth above, in further combination with WO 85/00112.

The teachings of EP, Knight, Radhakrishnan and Prince have been discussed above.

WO teaches the administration of vaporized microbicidal agent such as povidone-iodine for the treatment of the symptoms of a viral or bacterial infection. The administration is by nasal route (abstract and claims, claims 1 and 7 in particular).

It would have been obvious to one of ordinary skill in the art to administer the liposomal compositions containing povidone-iodine since the reference of WO shows that povidone-iodine can be administered safely by inhalation route to treat viral and bacterial infections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GS Kishore

Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK